Fibrodysplasia ossificans progressiva

Description

Fibrodysplasia ossificans progressiva is a disorder in which muscle tissue and connective tissue such as tendons and ligaments are gradually replaced by bone (ossified), forming bone outside the skeleton (extra-skeletal or heterotopic bone) that constrains movement. This process generally becomes noticeable in early childhood, starting with the neck and shoulders and proceeding down the body and into the limbs.

Extra-skeletal bone formation causes progressive loss of mobility as the joints become affected. Inability to fully open the mouth may cause difficulty in speaking and eating. Over time, people with this disorder may experience malnutrition due to their eating problems. They may also have breathing difficulties as a result of extra bone formation around the rib cage that restricts expansion of the lungs.

Any trauma to the muscles of an individual with fibrodysplasia ossificans progressiva, such as a fall or invasive medical procedures, may trigger episodes of muscle swelling and inflammation (myositis) followed by more rapid ossification in the injured area. Flare-ups may also be caused by viral illnesses such as influenza.

People with fibrodysplasia ossificans progressiva are generally born with malformed big toes. This abnormality of the big toes is a characteristic feature that helps to distinguish this disorder from other bone and muscle problems. Affected individuals may also have short thumbs and other skeletal abnormalities.

Frequency

Fibrodysplasia ossificans progressiva is a very rare disorder, believed to occur in approximately 1 in 2 million people worldwide. Several hundred cases have been reported.

Causes

Mutations in the *ACVR1* gene cause fibrodysplasia ossificans progressiva. This gene provides instructions for making a member of a protein family called bone morphogenetic protein (BMP) type I receptors. The ACVR1 protein is found in many tissues of the body including skeletal muscle and cartilage. It helps to control the growth and development of the bones and muscles, including the gradual replacement of cartilage by bone (ossification) that occurs in normal skeletal maturation from birth to

young adulthood.

Studies show that mutations in the *ACVR1* gene disrupt mechanisms that control the receptor's activity. As a result, the receptor is turned on when it normally should not be. Too much receptor activity causes overgrowth of bone and cartilage, resulting in the signs and symptoms of fibrodysplasia ossificans progressiva.

Learn more about the gene associated with Fibrodysplasia ossificans progressiva

- ACVR1

Inheritance

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Most cases of fibrodysplasia ossificans progressiva result from new mutations in the gene. These cases occur in people with no history of the disorder in their family. In a small number of cases, an affected person has inherited the mutation from one affected parent.

Other Names for This Condition

- FOP
- Myositis ossificans
- Myositis ossificans progressiva
- Progressive myositis ossificans
- Progressive ossifying myositis

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Progressive myositis ossificans (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0016037/)

Genetic and Rare Diseases Information Center

- Fibrodysplasia ossificans progressiva (https://rarediseases.info.nih.gov/diseases/6445/fibrodysplasia-ossificans-progressiva)

Patient Support and Advocacy Resources

- Disease InfoSearch (https://www.diseaseinfosearch.org/)

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov (https://clinicaltrials.gov/ct2/results?cond=%22fibrodysplasia+ossificans+progressiva%22+OR+%22Myositis+Ossificans%22)

Catalog of Genes and Diseases from OMIM

- FIBRODYSPLASIA OSSIFICANS PROGRESSIVA (https://omim.org/entry/135100)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28Myositis+Ossificans%5BMAJR%5D%29+AND+%28fibrodysplasia+ossificans+progressiva%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

References

- Fiori JL, Billings PC, de la Peña LS, Kaplan FS, Shore EM. Dysregulation ofthe BMP-p38 MAPK signaling pathway in cells from patients with fibrodysplasiaossificans progressiva (FOP). J Bone Miner Res. 2006 Jun;21(6):902-9. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16753021)
- Groppe JC, Shore EM, Kaplan FS. Functional modeling of the ACVR1 (R206H) mutation in FOP. Clin Orthop Relat Res. 2007 Sep;462:87-92. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17572636)
- Haupt J, Xu M, Shore EM. Variable signaling activity by FOP ACVR1 mutations. Bone. 2018 Apr;109:232-240. doi: 10.1016/j.bone.2017.10.027. Epub 2017 Oct 31. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/29097342) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5866189/)
- Hino K, Ikeya M, Horigome K, Matsumoto Y, Ebise H, Nishio M, Sekiguchi K, Shibata M, Nagata S, Matsuda S, Toguchida J. Neofunction of ACVR1 infibrodysplasia ossificans progressiva. Proc Natl Acad Sci U S A. 2015 Dec15;112(50):15438-43. doi: 10.1073/pnas.1510540112. Epub 2015 Nov 30. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/26621707) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4687587/)
- Kaplan FS, Glaser DL, Pignolo RJ, Shore EM. A new era for fibrodysplasiaossificans progressiva: a druggable target for the second skeleton. Expert OpinBiol Ther. 2007 May;7(5):705-12. Review. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17477807)
- O'Connell MP, Billings PC, Fiori JL, Deirmengian G, Roach HI, Shore EM, KaplanFS. HSPG modulation of BMP signaling in fibrodysplasia ossificans

progressivacells. J Cell Biochem. 2007 Dec 15;102(6):1493-503. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17516498)

- Olmsted EA, Kaplan FS, Shore EM. Bone morphogenetic protein-4 regulation infibrodysplasia ossificans progressiva. Clin Orthop Relat Res. 2003Mar;(408):331-43. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/12616078)
- Scarlett RF, Rocke DM, Kantanie S, Patel JB, Shore EM, Kaplan FS.Influenza-like viral illnesses and flare-ups of fibrodysplasia ossificansprogressiva. Clin Orthop Relat Res. 2004 Jun;(423):275-9. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15232462)
- Shore EM, Xu M, Feldman GJ, Fenstermacher DA, Cho TJ, Choi IH, Connor JM, Delai P, Glaser DL, LeMerrer M, Morhart R, Rogers JG, Smith R, Triffitt JT, Urtizberea JA, Zasloff M, Brown MA, Kaplan FS. A recurrent mutation in the BMPtype I receptor ACVR1 causes inherited and sporadic fibrodysplasia ossificansprogressiva. Nat Genet. 2006 May;38(5):525-7. Epub 2006 Apr 23. Erratum in: NatGenet. 2007 Feb;39(2):276. FOP International Research Consortium [removed]; Cho, Tae-Joon [added]; Choi, In Ho [added]; Connor, J Michael [added]; Delai, Patricia[added]; Glaser, David L [added]; LeMerrer, Martine [added]; Morhart, Rolf[added]; Rogers, John G [added]; Smith, Roger. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16642017)

Page last updated on 18 August 2020

Page last reviewed: 1 October 2019